REMARKS

I. Status of Claims

Upon entry of this amendment, claims 1, 5-11, 36-39, 41-46, and 49 are pending. Claim 47 has been cancelled. Claim 39 has been amended. The Office has indicated that claims 1 and 6-11 are allowed.

Cancellation of claim 47 is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the subject matter of the canceled claims.

Claim 39 has been amended to correct a typographical error. No new subject matter has been added, thus entry of this amendment is respectfully requested.

II. Withdrawn Rejections

Applicants acknowledge and thank the Examiner for withdrawing the rejection of claims 5, 36-39, 41-47, and 49 for failing to comply with the written description requirement for the reasons set forth on pages 4-5, section 7 of the Action mailed February 21, 2008 and for also withdrawing the rejection of claim 49 under 35 U.S.C. 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

III. Rejection under 35 U.S.C. § 112, First Paragraph, New Matter

The rejection of claim 47 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement and thus constituting new matter has been maintained. The Office maintains that the context of the claimed fragments recited in the specification at page 22 allegedly does not overlap with the claimed invention.

Given that claim 47 has been cancelled, Applicants respectfully assert that this rejection is now moot and respectfully request that this basis for rejection be withdrawn.

IV. Rejections - 35 U.S.C. § 112, First Paragraph, Enablement

Claims 5, 36-39, 41-47, and 49 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement In particular the Office alleges that undue experimentation would be required, because the specification fails to provide guidance as to how to make and use the broadly claimed nucleic acid molecules, and because there is no predictability as to which of the instantly claimed nucleic acid molecules will retain biological activity.

Applicants respectfully traverse the rejection and its supporting remarks.

The legal standard for determining enablement was established by the Supreme Court, in *Mineral Separation v. Hyde,* 242 U.S. 261, 270 (1916), to be whether undue or unreasonable experimentation is required to make and use the claimed invention. The Court in *In re Wands* indicated that undue experimentation should be evaluated based on eight factors. In making the instant rejection, the Office has asserted that undue experimentation would be required given the breadth of the claims, the lack of guidance provided and the lack of predictability. However, upon review of these factors, Applicants respectfully disagree.

Breadth of Claims

As an initial matter, Applicants respectfully point out that the instant claims do not include a functional limitation.

MPEP § 2164.08 states, "[t]hat claims are interpreted in light of the specification does not mean that everything in the specification must be read into the claims," quoting *Raytheon Co. v. Roper Corp.,* 724 F.2d 951, 957, 220 USPQ 592, 597 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984). Furthermore, "[l]imitations and examples in the specification do not generally limit what is covered by the claims."

It would appear that the Office is reading the functional limitations disclosed in the specification into the claims, given that the instant claims do not include a functional limitation. The specification provides ample support to enable the instantly claimed nucleic acid molecules. Therefore, the Office's assertions regarding the uncertainty of the functions or activities possessed by the claimed nucleic acid molecules are moot.

Guidance of the Specification

The Office alleges that the specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acids in a manner reasonably correlated with the broad scope of the claims.

35 U.S.C. § 112, first paragraph merely requires that the specification teach one of skill in the art how to make and use the invention. Furthermore, MPEP § 2164.01 (c) states that, "...when a compound or composition claim is not limited by a recited use, *any* enabled use that would reasonably correlate with the entire scope of the claim is sufficient to preclude a rejection for nonenablement based on how to use (emphasis added)." Thus, all that is required for enablement of the instantly claimed nucleic acid molecules is that the specification provide guidance for *making* the nucleic acid molecules and for at least one *use* for the nucleic acid molecules.

Guidance for the production of an isolated nucleic acid molecule comprising a polynucleotide that, except for no more than 5 or 3 conservative amino acid substitutions, encodes amino acids 1-273, 2-273, or 26-273 of SEQ ID NO: 2; comprising a polynucleotide at least 95% or 98% identical to a polynucleotide encoding amino acids 1-273, 2-273, or 26-273 of SEQ ID NO: 2 or a method of making a recombinant vector comprising inserting said polynucleotide into a vector; comprising a polynucleotide encoding a polypeptide at least 95% or 98% identical to SEQ ID NO: 2; or comprising a polynucleotide at least 95% or 98% identical to SEQ ID NO: 1 is provided throughout the instant specification. For example, paragraphs [0014]-[0015] and Figure 1 and 2 of the published application US2002/0004239 disclose the polynucleotide sequence of SEQ ID NO: 1 and the amino acid sequence of SEQ ID NO: 2. Furthermore, producing a defined variant of a

polynucleotide comprising SEQ ID NO: 1 or encoding a polypeptide comprising SEQ ID NO: 2 is well known in the art and routine. For example, paragraph [0069] discloses identifying polynucleotide variants of SEQ ID NO: 1 by using hybridization under stringent conditions to isolate the variants and using the Smith-Waterman algorithm to identify the percent identity of the variants to SEQ ID NO: 1; paragraph [0047] discloses which amino acid substitutions are conservative, and paragraph [0053] discloses using site-directed mutagenesis to produce polynucleotides that encode polypeptides comprising the amino acid substitutions; and paragraphs [0057]-[0058] disclose production of variant polypeptides by recombinant expression of the polynucleotide in prokaryotic or eukaryotic expression systems, or by chemical synthesis using solid phase peptide synthesis. The specification also provides guidance for at least one use of the instantly claimed nucleic acid molecules. For example, Example 2 and Table 2 of the published application disclose the use of a nucleic acid molecule as a marker for distinguishing between tumors that are likely to metastasize and those less likely to metastasize, by showing the differential expression of the nucleic acid molecule in highly metastatic versus non-metastatic breast cancer cell lines. Furthermore, paragraphs [0064] and [0065] describe using polypeptides encoded by the claimed nucleic acids to produce antibodies using standard methods. For example, polypeptides can be used to immunize a rabbit and then antisera can be collected from the immunized rabbit.

The Office further alleges that since there is no guidance in the specification regarding the use of divergent sequences, the instantly claimed nucleic acids will encode proteins that may not maintain the activity of a marker for distinguishing between tumors that are likely to metastasize and those less likely to metastasize. MPEP § 2164.08(b) makes clear that, "[t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art," quoting *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984).

Given the state of the art regarding methods for screening and identifying nucleic acid molecules, one of ordinary skill in the art could determine which of the conceived embodiments would be inoperative or operative as a marker of tumor metastasis without undue experimentation. Routine methods well known in the art could be used to identify and screen for the operative embodiments of the claimed nucleic acid molecules. For example, nucleic acid molecules can be screened for their use as a marker of tumor metastasis by using Northern blots to detect the mRNA levels of the nucleic acid molecules, as disclosed in paragraph [0048] of the published application US2002/0004239.

Predictability of Whether Claimed Nucleic Acids Encode Polypeptides with Biological Activity

Finally, the Office alleges that the encoded polypeptides may not maintain the activities proposed in the specification and that there is no predictability with regard to what changes can be made to the claimed nucleic acid molecules while maintaining biological activity. Again, because the instant claims do not include a functional limitation, whether the claimed nucleic acid molecules encode polypeptides retaining biological activity per se is moot.

Further, that Office is reminded that even if the claims included a functional limitation, complete predictability is not required to enable a claimed invention. With regard to the Office's assertion that there is no guidance to predict which of the "infinite possible choices" of conservative amino acid substitutions within the claimed range of amino acids 1-273, 2-273, or 26-273 of SEQ ID NO: 2 would be successful, Applicants respectfully point out that, as discussed above, even if some of the embodiments were inoperative, that would not necessarily render the claims nonenabled. The specification provides ample support for producing a nucleic acid molecule that encodes a polypeptide comprising the amino acid substitutions, for example paragraphs [0047] and [0053] of the published application US2002/0004239, and for comparing the sequence of the polypeptide to SEQ ID NO: 2 to determine where the substitution(s) occurs, for example paragraph

[0046]. Furthermore, given that the claims do not include a functional limitation, the teachings of the Lazar article are moot.

Conclusion

Given that the instant claims do not recite a functional limitation and that the specification provides guidance for how to make and use the instant nucleic acid molecules commensurate with the scope of the claims, the experimentation required to make and use the instantly claimed invention would not be undue. Applicants respectfully assert that instant claims 5, 36-39, 41-46, and 49 are enabled under 35 U.S.C. § 112, first paragraph. Therefore, Applicants respectfully request that this basis for rejection be withdrawn.

V. Rejection under 35 U.S.C. § 112, Second Paragraph, Indefiniteness

The rejection of claim 47 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been maintained. The Office maintains that claim 47 allegedly implies that the claimed fragment encodes the portions of SEQ ID NO: 2 listed in any one of claims 5, 36, or 39.

Given that claim 47 has been cancelled, Applicants respectfully assert that this rejection is now moot and request that this basis for rejection be withdrawn.

VI. Allowable Subject Matter

The Office states that claims 1 and 7-11 are allowed. However, the Office Action Summary states that claims 1 and *6-11* are allowed. Based on the Office Action mailed February 21, 2008, and the fact that the Office has not stated any new grounds for rejection of claim 6 in the instant Office Action; Applicants assume the Office meant to state that claims 1 and 6-11 are allowed.

VII. Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. **03-1952** referencing docket no. **223002105400**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

In addition, please direct all further communications in this application to:

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Respectfully submitted,

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